行政院國家科學委員會專題研究計畫成果報告

序貫實驗之參數估計
Estimation after sequential experiments

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一、中文摘要

對於任一實驗,如其實驗之自變數在下一時間點所選取的值,可由過去的實驗值來決定,則稱之為序貫設計的實驗.常見的例子如臨床試驗，其中需要比較兩種或多種藥物的優劣，基於醫德上的考量，若實驗初期即明顯可見優劣差別，實驗者必須盡早做出決定，避免劣藥試驗於更多病人.通常一個好的序貫設計的實驗有助於提高實驗的效率,但是它付出的代價是使得參數的估計變得複雜許多,傳統推導信賴區間的方法所針對的是固定樣本的實驗.

本人與 Woodroofe [4]將 very weak expansions 理論推廣到多變數指數族,我們並對 Poisson 分佈作模擬,實驗結果顯示此理論相當準確. 在這計畫中,我將此一理論應用到二項分佈, 並比較模擬結果與理論結果.

關鍵詞：序貫估計 二項式分佈 指數族 非常弱展開法

Abstract

Consider a sequential trial comparing two treatments with binary responses. We assume that sampling follows some symmetric random scheme so that the sample sizes are about equal in the two populations. After such a trial, the confidence interval estimation for a treatment difference is often of interest. In this project we apply and extend Weng and Woodroofe's [5] procedure to this estimation problem. Examples such as symmetric triangular tests and sequential probability ratio test with parallel stopping boundaries are provided to illustrate the application of this method. The performance is assessed through simulation studies of coverage probabilities. This technique is also used to set confidence sets for the absolute success probabilities.

Keywords: sequential estimations, binomial distribution, exponential families, very weak expansions

二、Introduction

Consider a sequential clinical trial comparing an experimental treatment with a control. Assume that the outcomes are dichotomous and the results are known immediately. A variety of sequential designs have been proposed to detect a difference in the means of the two binomial populations. We denote the parameter of true treatment difference as Δ and test H0: $\Delta = 0$ versus H1: $\Delta > 0$ sequentially. After such a test, it is desirable to obtain accurate confidence limits for Δ and for functions of parameters, such as absolute success probabilities. These are our main concerns.

三、Main results

Suppose that the experiments are run in a sequential manner with a total of n patients, of them n1 were randomized to the experimental treatment and n2=n-n1 were randomized to

the control. Let Y1j, j=1,…,n1, denote the binary outcome of the j-th patient receiving the experimental treatment that takes value 1 if the treatment is successful and 0 otherwise. Similarly let Y2k, k=1,…,n2, be the binary patient outcome from the control. All responses are assumed to be independent. The two values of a binary patient response are referred to as ``success" and ``failure" and the success probabilities of experimental treatment and of control are denoted as p1 and p2, respectively, where 0< p1,p2 < 1 are unknown. We take the log-odds-ratio as a measure of treatment effect and write

$\boldsymbol{D}$=log {p_1 (1-p_2)/[(1-p_1) p_2]}.

The null hypothesis H0: $\boldsymbol{D} = 0$ is tested against the alternative H1: $\boldsymbol{D} > 0$ sequentially.

For the estimation problem after sequential tests, Todd, Whitehead, and Facey [4] and Todd and Whitehead [3] proposed to modify Woodroofe's [6] approximate theory method and use the efficient score statistic and Fisher's information. To derive a refined pivot, calculations of expectations of functions of the two statistics are required. They suggested a method to evaluate these expectations by incorporating a recursive numerical integration. However, this method requires knowledge of the complete inspection schedule and the complete sample paths associated with every stopping point on the boundary, which causes the computation time to be prohibitive. Consequently, two contrasting assumptions referred to as ``equal inspection" and ``one last inspection" are made. These assumptions are disconcerting as they pointed out.

We propose to adapt the method of Weng and Woodroofe [4] by first defining an approximate pivot Z and then setting confidence sets based on a refined pivot Z*, where refined pivot is obtained by mean and variance corrections. Suppose that the trial has been carried out sequentially until certain stopping boundaries are crossed. Since the use of sequential method does not affect the form of the likelihood, the likelihood function can be easily written down. From this the initial pivot is defined through the signed-root transformation as in Barndorff-Nielsen [1] and Bickel and Ghosh [2].

Although the original form of Weng and Woodroofe's [5] results requires equal sizes in the two populations, we extend the results to situations where each patient is allowed to be randomized to either population at equal rates. The reasons supporting this extension are as below. 1, Of course the initial pivot Z will change, but the mathematical arguments involved are essentially the same. 2. The forms of the mean and variance corrections are not sensitive to the use of a symmetric random scheme.

The advantage of using this transformation is that expectations of some functions of the terminal values of this pivot can be derived in explicit forms. So a refined pivot can be obtained easier and the implementation is computationally inexpensive.

四、Conclusions

In this report we have summarized our past efforts on the problem of estimation after sequential tests. Through the simulation, we found that the proposed approach provides pretty good approximations to the coverage probabilities. One of my students is continuing to work on this area where the treatments are allowed to be more than two.

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六、Bibliography

[1] Ole. Barndorff-Nielsen. "Inference for full or partial parameters based on the standardized signed log likelihood ratio," *Biometrika*, 73 (1986), 307-322.

[2] P. Bickel and J. K. Ghosh. "A decomposition for the likelihood ratio statistic and the Bartlett correction--A Bayesian

argument," *Ann. Statist.,* 18 (1990), 1070-1090.

[3] S. Todd and J. Whitehead. "Confidence interval calculation for a sequential clinical trial of binary responses," *Biometrika*, 84 (1997), 737-743.

[4] S. Todd, J. Whitehead, and K. M. Facey. "Point and interval estimation following a sequential clinical trial," *Biometrika*, 83 (1996), 453-461.

[5] R. C. Weng and M. Woodroofe. "Integrable expansions for posterior distributions for multiparameter exponential families with applications to sequential confidence levels," *Statistica Sinica*, 10 (2000), 693-713.

[6] M. Woodroofe. "Estimation after sequential testing: A simple approach for a truncated sequential probability ratio test," *Biometrika*, 79 (1992), 347-353.